REMARKS

Claims 1-15 are all the claims pending in the application. Claims 1 and 16 are amended herein to exclude unsubstituted pyridyl groups as substituents for the recited "J" variable and to delete the provisos added in the Amendment filed on December 17, 2001. Applicants submit that negative limitations or provisos excluding alternative elements are adequately supported by the specification where the excluded element is positively recited. *See* MPEP 2173.05(i). Therefore, support for the amendment to claims 1 and 16 to exclude unsubstituted pyridyl groups can be found on page 15 where unsubstituted pyridyl groups are disclosed as alternative substituents for the "J" variable, e.g., J76, J77, J78 and J79, and on page 16 where specific compounds using J76, J77, J78 and J79 as the "J" variable are disclosed.

I. Claim Rejections Under 35 USC 112, 2nd paragraph

Claims 13 and 15-17 are rejected under 35 U.S.C. § 112, 2nd paragraph as allegedly being indefinite. Specifically the Examiner indicates:

a. Claim 13 is dependent on the canceled claim 12 and is dependent on itself;

b. In claims 16, 17, the subject to whom the composition is administered is required and a "biologically effective amount" is not defined;

c. In claims 13, and 15-17, is not clear what the conditions are wherein a disease is prevented and/or treated or what is intended for a "disease of the respiratory organs, a disease of the circulatory organs, a disease of bone/cartilage metabolism"?

Claim 13 is amended herein to depend on claims 1-11, thereby obviating the rejection with respect to claim 13.

With respect to the subject to whom the composition is administered and the terms "biologically effective amount", Applicants respectfully submit that the claims are clear and definite within the meaning 32 USC 112, 2nd paragraph when properly read in light of the specification. The Examiner's focus in determining whether the claims are definite in compliance with 35 U.S.C. § 112, second paragraph should be whether the claims set out the claimed subject matter with a reasonable degree of clarity and particularity in light of (1) the content of the specification; (2) the teachings of the prior art; and (3) the claim interpretation that would be given by one of ordinary skill in the art. In this case, the specification discloses that the claimed compound inhibits "human" chymase activity and an approximate dosage range (page 66, lines 5-13). Thus, when read in light of the specification one of ordinary skill in the art would be able to determine the scope of the claims and to practice the claimed invention.

With respect to the rejection of the recitation of "disease of respiratory organs, a disease of circulatory organs, or a disease of bone/cartilage metabolism," Applicants submit that the claim is definite within the meaning of 35 USC 112, 2nd paragraph when read in light of the specification as discussed above. Specifically, examples of the recited disease conditions are disclosed on page 1, lines 27-36, i.e., diseases of the respiratory organs, such as bronchial asthma; diseases of circulatory organs for example sclerosing vascular lesions, intravascular stenosis, disturbances of peripheral circulation, renal failure and cardiac failure; and diseases of bone/cartilage metabolism such as rheumatoid arthritis and osteoarthritis.

In view of the above, Applicants respectfully request withdrawal of the rejections.

II. Claim Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 1-11, 13 and 15-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which is not enabled by the specification. Specifically, the Examiner refers to the proviso added in claim 1 in the Amendment filed on December 17, 2001, and states that the following are not described in the specification: the specific compound wherein m=0, A is an alkylene, J represents 2, 5-dimethylimidazole-4-yl, G = $-CH_2-$; the specific compound wherein J is alkylene, A is a pyrimidine ring and the position of the pyrimidine ring binds to the methylene adjacent to the S in formula (1); and the specific compound wherein m is 1 or 2, J represents 2, 5-dimethylimidazole-4-yl, G = $-CH_2-$ or J is alkylene, A is a pyrimidine ring and the position of the pyrimidine ring binds to the methylene adjacent to the S in formula (1).

Applicants submit that when the number of carbon atoms in the cyclic structures, i.e., an "aryl", and "heteroaryl", is defined in the claims and specification, the number of carbons correctly means the number of ring carbons, excluding carbons of a substituent group. For example, although the methyl benzene structure has 7 carbons, the benzene structure does not fall under the definition of "an aryl group having 7 to 9 carbons." Similarly, although a dimethyl imidazole group has a total of 5 carbon atoms, the imidazole ring only has 3 carbon atoms. Therefore a dimethyl imidazole group does not fall under a "heteroaryl group having 4 to 11 carbons." In this regard, Applicants have amended claim 1, thereby clarifying the claimed invention. Accordingly, Applicants respectfully request withdrawal of the rejection.

III. Claim Rejections Under 35 U.S.C. § 103

A. Bru-Magniez I, II and III

The rejection over Bru-Magniez I (5021443, PTO 1449), or Bru-Magniez II (5021443) is maintained for reasons of record and is applied to new claims 16-17.

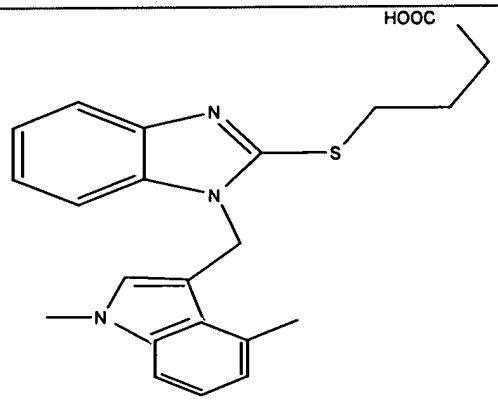
Applicants respectfully traverse the rejection and submit that the Bru-Magniez references do not teach or suggest the presently claimed invention. The Bru-Magniez references teach compounds having a benzene ring having a substituent group, such as a methyl group. On the other hand, the first definition of "J" in the present invention reads "when m is 0 and A is a substituted or unsubstituted, linear or branched alkylene group having 1 to 6 carbons, then J represents . . . a substituted or unsubstituted aryl group having 7 to 9 carbons." In this case, the definition does not include a benzene ring having 6 carbon atoms even if the benzene ring is substituted with a carbon-containing substituent group.

Applicants further submit that the compounds of the present invention have chymase inhibitory activity, while the compounds disclosed in the Bru-Magniez references have TXA_2 receptor inhibitory activity. As discussed above, the structure of the chymase and that of the TXA_2 receptor are different, and therefore, the references do not suggest the compounds of the present invention having chymase inhibitory activity. In addition, the compounds of the present invention are characterized by having the "S" atom bonded at the 2 position of the benzimidazole ring. On the other hand, according to the Bru Magniez reference, US 5,012, 443, compounds having "S" at the corresponding position have rather low TXA_2 receptor inhibitory activity. Therefore, one of ordinary skill in the art would not have had a reasonable expectation

of success of achieving the claimed inventions, the recited compounds having chymase inhibitory activity on the basis on the TXA_2 receptor inhibitory activity. Thus, the Examiner has not made a *prima facie* showing of obviousness.

In addition, compounds of the presently claimed invention exhibit unexpectedly superior properties. For example, the compound of the present invention, shown in the following Table has very high chymase inhibitory activity, but has very low TXA_2 receptor inhibitory activity.

TABLE

Structure	Chymase IC_{50} (M)	TXA_2 receptor 10^{-8}M (%)	10^{-7}M (%)	10^{-6}M (%)
	7.52×10^{-9}	0.00	21.97	57.08

As can be seen from the above Table, the chymase inhibitory activity of the claimed compounds of the present invention is about 1000 times higher that its TXA_2 receptor inhibitory activity. This data shows that there is no relationship between the chymase inhibitory activity and the TXA_2 receptor inhibitory activity.

Therefore, as shown and discussed above, the Bru Magniez references do not teach or suggest the presently claimed compounds having chymase inhibitory activity. Accordingly, Applicants respectfully request withdrawal of the rejection.

B. JP-1265089

Claims 1, 2, and 8-15 were rejected under 35 U.S.C. 103(a) as being unpatentable over JP-1265089.

Applicants submit that JP-1265089 teaches compounds having an imidazole structure having three carbons and does not teach or suggest the presently claimed compounds recited in claim 1, as amended, or their activity as human chymase inhibitors. Specifically, the disclosed compounds are disclosed as having anti-ulcer activity, however, there is no disclosure or suggestion that the disclosed compounds have chymase inhibitory activity. According to the description in JP '089, it appears as if the disclosed compounds described in this reference having a lower alkyl as $-Z-R^2$ has higher anti-ulcer activity. However, the compounds of the present invention do not have a lower alkyl group at the position corresponding to the - $Z-R^2$ in the JP '089 reference. Therefore, JP '089 does not suggest the present invention compounds having chymase inhibitory activity.

Accordingly, Applicants respectfully request withdrawal of the rejection.

C. JP 05-112559

Claims 1-12 were rejected under 35 U.S.C. 103(a) as being unpatentable over Shimamura (JP 05-112559).

Applicants respectfully submit that Shimamura does not teach or suggest the presently claimed compounds recited in amended claim 1 or their activity as human chymase inhibitors. Specifically, the disclosed compounds are disclosed as having anti-ulcer activity, however, there is no disclosure or suggestion that the disclosed compounds have chymase inhibitory activity.

Therefore, JP '089 does not suggest the present inventive compounds having chymase inhibitory activity.

Accordingly, Applicants respectfully request withdrawal of the rejection.

V. Information Disclosure Statement

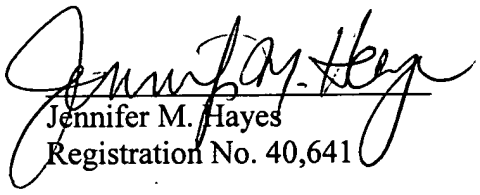
Applicants submit herewith an Information Disclosure Statement listing JP 62212386 which describes compounds having an unsubstituted pyridyl group at the position corresponding to "J" of the formula (1) of the present invention. The presently claimed compounds are distinguished over the compounds disclosed by JP '386. Further, the disclosed compounds are described as having anti-ulcer activity, but are not disclosed as having chymase inhibitory activity. Therefore JP '386 doses not teach or suggest the presently claimed invention.

VI. Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

Applicant hereby petitions for any extension of time which may be required to maintain the pendency of this case, and any required fee, except for the Issue Fee, for such extension is to be charged to Deposit Account No. 19-4880.

Respectfully submitted,



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APPENDIX

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

The specification is changed as follows:

On page 4, paragraph 2, beginning at line 6:

when m is 0 and A is a substituted or unsubstituted, linear or branched alkylene group having 1 to 6 carbons, then J represents a substituted or unsubstituted, linear, cyclic or branched alkyl group having 3 to 6 carbons, a substituted or unsubstituted aryl group having 7 to 9 carbons, a substituted aryl group having 10 to 11 carbons, a substituted or unsubstituted heteroaryl group (excluding unsubstituted pyridyl groups) having 4 to 10 carbons that may contain one or a plurality of oxygen, nitrogen and sulfur atoms on the ring;

On page 4, paragraph 3, beginning at line 16:

when m is 0 and A is a substituted or unsubstituted arylene group having 6 to 11 carbons or a substituted or unsubstituted heteroarylene group having 4 to 10 carbons that may contain one or a plurality of oxygen, nitrogen and sulfur atoms on the ring, then J represents a substituted or unsubstituted, linear, cyclic or branched alkyl group having 1 to 6 carbons, a substituted or unsubstituted aryl group having 6 to 11 carbons, or a substituted or unsubstituted heteroaryl group (excluding unsubstituted pyridyl groups) having 4 to 10 carbons that may contain one or a plurality of oxygen, nitrogen and sulfur atoms on the ring; or

On page 4, the last paragraph bridging pages 4 and 5:

when m is 0 and A is a single bond or when m is 1 or 2, then J represents a substituted or unsubstituted, linear, cyclic or branched alkyl group having 1 to 6 carbons, a substituted or

unsubstituted aryl group having 6 to 11 carbons, or a substituted or unsubstituted heteroaryl group (excluding unsubstituted pyridyl groups) having 4 to 10 carbons that may contain one or a plurality of oxygen, nitrogen and sulfur atoms on the ring, in which the substituent represents a halogen atom, OH, NO_2, CN, a linear or branched alkyl group having 1 to 6 carbons, a linear or branched alkoxy group having 1 to 6 carbons (the substituents may be joined to each other at adjacent sites via an acetal bond), a linear or branched alkylthio group having 1 to 6 carbons, a linear or branched alkylsulfonyl group having 1 to 6 carbons, a linear or branched acyl group having 1 to 6 carbons, a linear or branched acylamino group having 1 to 6 carbons, a substituted or unsubstituted anilide group, a trihalomethyl group, a trihalomethoxy group, a phenyl group, an oxo group, a $COOR^3$ group, or a phenoxy group that may be substituted with one or more halogen atoms, and in which the substituents may be independently substituted at any one or more sites of the ring or the alkylene group; and

On page 10, the third paragraph bridging pages 10 and 11:

When m is 0 and A is a substituted or unsubstituted, linear or branched alkylene group having 1 to 6 carbons, then J represents a substituted or unsubstituted, linear, cyclic or branched alkyl group having 3 to 6 carbons, a substituted or unsubstituted aryl group having 7 to 9 carbons, a substituted aryl group having 10 to 11 carbons, a substituted or unsubstituted heteroaryl group (excluding unsubstituted pyridyl groups) having 4 to 10 carbons that may contain one or a plurality of oxygen, nitrogen and sulfur atoms on the ring. Preferably, a substituted aryl group having 10 to 11 carbons and a substituted or unsubstituted heteroaryl group having 4 to 10 carbons that may contain one or a plurality of oxygen, nitrogen and sulfur

atoms on the ring may be mentioned. As the substituted or unsubstituted, linear, cyclic or branched alkyl group having 1 to 6 carbons, there can be mentioned a (n, i-) propyl group, a (n, i, s, t-) butyl group, a (n, i, ne, t-) pentyl group and a cyclohexyl group. As the substituted or unsubstituted aryl group having 7 to 9 carbons, there can be mentioned an indenyl group, and as the substituted aryl group having 10 to 11 carbons, there can be mentioned a naphthyl group. As the substituted or unsubstituted heteroaryl group having 4 to 10 carbons that may contain one or a plurality of oxygen, nitrogen and sulfur atoms on the ring, there can be mentioned a pyridyl group, a furanyl group, a thiophenyl group, an imidazole group, a thiazole group, a pyrimidine group, an oxazole group, an isoxazole group, a benzofurane group, a benzimidazole group, a quinoline group, an isoquinoline group, a quinoxaline group, a benzoxadiazole group, a benzothiadiazole group, an indole group, a N-methylindole group, a benzothiazole group, a benzothiophenyl group, a benzisoxazole group and the like, and preferably a benzothiophenyl group or a N-methylindole group may be mentioned.

On page 11 the paragraph bridging pages 11 and 12:

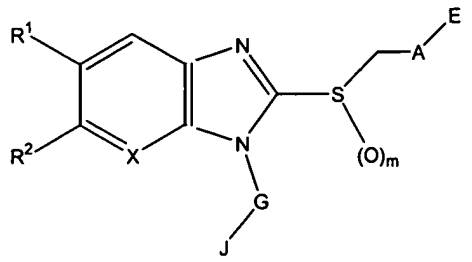
When m is 0 and A is a substituted or unsubstituted arylene group having 6 to 11 carbons or a substituted or unsubstituted heteroarylene group having 4 to 10 carbons that may contain one or a plurality of oxygen, nitrogen and sulfur atoms on the ring, then J represents a substituted or unsubstituted, linear, cyclic or branched alkyl group having 1 to 6 carbons, a substituted or unsubstituted aryl group having 6 to 11 carbons, or a substituted or unsubstituted heteroaryl group having 4 to 10 carbons that may contain one or a plurality of oxygen, nitrogen and sulfur atoms on the ring, and preferably a substituted or unsubstituted aryl group having 6 to 11 carbons

and a substituted or unsubstituted heteroaryl group (excluding unsubstituted pyridyl groups) having 4 to 10 carbons that may contain one or a plurality of oxygen, nitrogen and sulfur atoms on the ring may be mentioned. As the substituted or unsubstituted aryl group having 6 to 11 carbons, there can be mentioned a phenyl group, an indenyl group, a naphthyl group and the like, and preferably a phenyl group or a naphthyl group may be mentioned. As the substituted or unsubstituted, linear, cyclic or branched alkyl group having 1 to 6 carbons and as the substituted or unsubstituted heteroaryl group having 4 to 10 carbons that may contain one or a plurality of oxygen, nitrogen and sulfur atoms on the ring, there can be mentioned those described above. As the substituent as used herein, there can be mentioned a halogen atom, OH, NO_2, CN, a linear or branched alkyl group having 1 to 6 carbons, a linear or branched alkoxy group having 1 to 6 carbons (the substituents may be joined to each other at adjacent sites via an acetal bond), a linear or branched alkylthio group having 1 to 6 carbons, a linear or branched alkylsulfonyl group having 1 to 6 carbons, a linear or branched acyl group having 1 to 6 carbons, a linear or branched acylamino group having 1 to 6 carbons, a substituted or unsubstituted anilide group, a 20 trihalomethyl group, a trihalomethoxy group, a phenyl group, or a phenoxy group that may be substituted with one or more halogen atoms. They may be independently substituted at any one or more sites of the ring or the alkyl group. Specifically, there can be mentioned OH, a chloro group, a bromo group, a nitro group, a methoxy group, a cyano group, a methylenedioxy group, a trifluoromethyl group, a trifluoromethoxy group, a methyl group, an ethyl group, a (n, i-) propyl group, a (n, i, s, t-) butyl group, an anilide group and the like.

IN THE CLAIMS:

The claims are amended as follows:

1. (Twice Amended) A thiobenzimidazole compound represented by the following formula (1):



(1)

wherein,

R^1 and R^2, simultaneously or independently of each other, represent a hydrogen atom, a halogen atom, a trihalomethyl group, a cyano group, a hydroxy group, an alkyl group having 1 to 4 carbons or an alkoxy group having 1 to 4 carbons, or R^1 and R^2 together form -O-CH_2-O-, -O-CH_2-CH_2-O- or -CH_2-CH_2-CH_2-, in which the carbons may be substituted with one or a plurality of alkyl groups having 1 to 4 carbons;

A represents a single bond, a substituted or unsubstituted, linear or branched alkylene group having 1 to 6 carbons, a substituted or unsubstituted arylene group having 6 to 11 carbons, or a substituted or unsubstituted heteroarylene group having 4 to 10 carbons that may contain one or a plurality of oxygen, nitrogen and sulfur atoms on the ring, in which the substituent represents a halogen atom, OH, NO_2, CN, a linear or branched alkyl group having 1 to 6 carbons, a linear or branched alkoxy group having 1 to 6 carbons (the substituents may be joined to each

other at adjacent sites via an acetal bond), a linear or branched alkylthio group having 1 to 6 carbons, a linear or branched alkylsulfonyl group having 1 to 6 carbons, a linear or branched acyl group having 1 to 6 carbons, a linear or branched acylamino group having 1 to 6 carbons, a trihalomethyl group, a trihalomethoxy group, a phenyl group, an oxo group, or a phenoxy group that may be substituted with one or more halogen atoms, and in which the substituents may be independently substituted at any one or more sites of the ring or the alkylene group;

E represents $COOR^3$, SO_3R^3, $CONHR^3$, SO_2NHR^3, a tetrazole group, a 5-oxo-1,2,4-oxadiazole group or a 5-oxo-1,2,4-thiadiazole group in which R^3 represents a hydrogen atom, or a linear or branched alkyl group having 1 to 6 carbons;

G represents a substituted or unsubstituted, linear or branched alkylene group having 1 to 6 carbons that may be interrupted with one or a plurality of O, S, SO_2, and NR^3, in which R^3 is as defined above and the substituent represents a halogen atom, OH, NO_2, CN, a linear or branched alkyl group having 1 to 6 carbons, a linear or 15 branched alkoxy group having 1 to 6 carbons (the substituents may be joined to each other at adjacent sites via an acetal bond), a trihalomethyl group, a trihalomethoxy group, a phenyl group, or an oxo group;

m represents an integer of 0 to 2;

when m is 0 and A is a substituted or unsubstituted, linear or branched alkylene group having 1 to 6 carbons, then J represents a substituted or unsubstituted, linear, cyclic or branched alkyl group having 3 to 6 carbons, a substituted or unsubstituted aryl group having 7 to 9 carbons, a substituted aryl group having 10 to 11 carbons, a substituted or unsubstituted heteroaryl group (excluding unsubstituted pyridyl groups) having 4 to 10 carbons that may

contain one or a plurality of oxygen, nitrogen and sulfur atoms on the ring~~, with the proviso that J does not represent 2,5-dimethylimidazole-4-yl, when G represents $-CH_2-$~~;

when m is 0 and A is a substituted or unsubstituted arylene group having 6 to 11 carbons or a substituted or unsubstituted heteroarylene group having 4 to 10 carbons that may contain one or a plurality of oxygen, nitrogen and sulfur atoms on the ring, then J represents a substituted or unsubstituted, ~~linear,~~ cyclic ~~or branched~~ alkyl group having 1 to 6 carbons, a substituted or unsubstituted aryl group having 6 to 11 carbons, or a substituted or unsubstituted heteroaryl group (excluding unsubstituted pyridyl groups) having 4 to 10 carbons that may contain one or a plurality of oxygen, nitrogen and sulfur atoms on the ring~~, with the proviso that J does not represent unsubstituted, linear or branched alkyl groups having 1 to 6 carbon atoms, when A represents a pyrimidine ring and the position 2 of the pyrimidine ring binds to the methylene adjacent to the S in the formula (1)~~; or

when m is 0 and A is a single bond or when m is 1 or 2, then J represents a substituted or unsubstituted, ~~linear,~~ cyclic ~~or branched~~ alkyl group having 1 to 6 carbons, a substituted or unsubstituted aryl group having 6 to 11 carbons, or a substituted or unsubstituted heteroaryl group (excluding unsubstituted pyridyl groups) having 4 to 10 carbons that may contain one or a plurality of oxygen, nitrogen and sulfur atoms on the ring, in which the substituent represents a halogen atom, OH, NO_2, CN, a linear or branched alkyl group having 1 to 6 carbons, a linear or branched alkoxy group having 1 to 6 carbons (the substituents may be joined to each other at adjacent sites via an acetal bond), a linear or branched alkylthio group having 1 to 6 carbons, a linear or branched alkylsulfonyl group having 1 to 6 carbons, a linear or branched acyl group

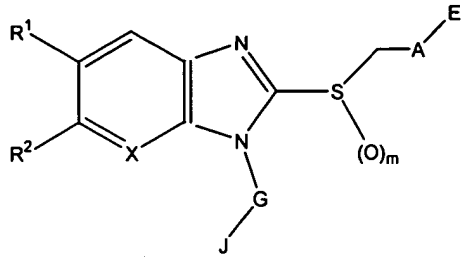
having 1 to 6 carbons, a linear or branched acylamino group having 1 to 6 carbons, a substituted or unsubstituted anilide group, a trihalomethyl group, a trihalomethoxy group, a phenyl group, an oxo group, a $COOR^3$ group, or a phenoxy group that may be substituted with one or more halogen atoms, and in which the substituents may be independently substituted at any one or more sites of the ring or the alkylene group, ~~with the proviso that J does not represent 2,5-dimethylimidazole-4-yl, when m is 0, A is a single bond, and G represents $-CH_2-$; and further with the proviso that J does not represent unsubstituted, linear or branched alkyl groups having 1 to 6 carbon atoms, when A represents a pyrimidine ring and the position 2 of the pyrimidine ring binds to the methylene adjacent to the S in the formula (1)~~; and

X represents CH or a nitrogen atom;

or a medically acceptable salt thereof.

13. (Amended) A pharmaceutical composition which is a preventive ~~and/~~or therapeutic agent of a disease comprising at least one human chymase inhibitor thiobenzimidazole compound according to any one of claims ~~1 to 13~~1 to 11 or a medically acceptable salt thereof and a pharmaceutically acceptable carrier.

16. (Amended) A method for inhibiting human chymase comprising administering to a human subject an ~~a biologically~~ effective amount of a pharmaceutical composition comprising a thiobenzimidazole compound as the active ingredient represented by the following formula (1):



(1)

wherein, R^1 and R^2, simultaneously or independently of each other, represent a hydrogen atom, a halogen atom, a trihalomethyl group, a cyano group, a hydroxy group, an alkyl group having 1 to 4 carbons or an alkoxy group having 1 to 4 carbons, or R^1 and R^2 together form -O-CH_2-O-, -O-CH_2-CH_2-O- or -CH_2-CH_2-CH_2-, in which the carbons may be substituted with one or a plurality of alkyl groups having 1 to 4 carbons;

A represents a single bond, a substituted or unsubstituted, linear or branched alkylene group having 1 to 6 carbons, a substituted or unsubstituted arylene group having 6 to 11 carbons, or a substituted or unsubstituted heteroarylene group having 4 to 10 carbons that may contain one or a plurality of oxygen, nitrogen and sulfur atoms on the ring, in which the substituent represents a halogen atom, OH, NO_2, CN, a linear or branched alkyl group having 1 to 6 carbons, a linear or branched alkoxy group having 1 to 6 carbons (the substituents may be joined to each other at adjacent sites via an acetal bond), a linear or branched alkylthio group having 1 to 6 carbons, a linear or branched alkylsulfonyl group having 1 to 6 carbons, a linear or branched acyl group having 1 to 6 carbons, a linear or branched acylamino group having 1 to 6 carbons, a trihalomethyl group, a trihalomethoxy group, a phenyl group, an oxo group, or a phenoxy group that may be substituted with one or more halogen atoms, and in which the substituents may be independently substituted at any one or more sites of the ring or the alkylene group;

E represents $COOR^3$, SO_3R^3, $CONHR^3$, SO_2NHR^3, a tetrazole group, a 5-oxo-1,2,4-

oxadiazole group or a 5-oxo-1,2,4-thiadiazole group in which R^3 represents a hydrogen atom, or a linear or branched alkyl group having 1 to 6 carbons;

G represents a substituted or unsubstituted, linear or branched alkylene group having 1 to 6 carbons that may be interrupted with one or a plurality of O, S, SO_2, and NR^3, in which R^3 is as defined above and the substituent represents a halogen atom, OH, NO_2, CN, a linear or branched alkyl group having 1 to 6 carbons, a linear or 15 branched alkoxy group having 1 to 6 carbons (the substituents may be joined to each other at adjacent sites via an acetal bond), a trihalomethyl group, a trihalomethoxy group, a phenyl group, or an oxo group;

m represents an integer of 0 to 2;

when m is 0 and A is a substituted or unsubstituted, linear or branched alkylene group having 1 to 6 carbons, then J represents a substituted or unsubstituted, linear, cyclic or branched alkyl group having 3 to 6 carbons, a substituted or unsubstituted aryl group having 7 to 9 carbons, a substituted aryl group having 10 to 11 carbons, a substituted or unsubstituted heteroaryl group (excluding unsubstituted pyridyl groups) having 4 to 10 carbons that may contain one or a plurality of oxygen, nitrogen and sulfur atoms on the ring~~, with the proviso that J does not represent 2,5-dimethylimidazole-4-yl, when G represents $-CH_2-$~~;

when m is 0 and A is a substituted or unsubstituted arylene group having 6 to 11 carbons or a substituted or unsubstituted heteroarylene group having 4 to 10 carbons that may contain one or a plurality of oxygen, nitrogen and sulfur atoms on the ring, then J represents a substituted or unsubstituted, ~~linear,~~ cyclic ~~or branched~~ alkyl group having 1 to 6 carbons, a substituted or unsubstituted aryl group having 6 to 11 carbons, or a substituted or unsubstituted

heteroaryl (excluding unsubstituted pyridyl groups) group having 4 to 10 carbons that may contain one or a plurality of oxygen, nitrogen and sulfur atoms on the ring~~, with the proviso that J does not represent unsubstituted, linear or branched alkyl group having 1 to 6 carbon atoms, when A represents a pyrimidine ring and the position 2 of the pyrimidine ring binds to the methylene adjacent to the S in the formula (1)~~; or

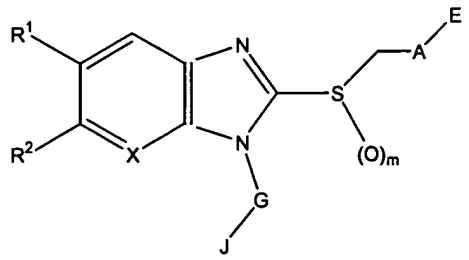
when m is 0 and A is a single bond or when m is 1 or 2, then J represents a substituted or unsubstituted~~, linear,~~ cyclic ~~or branched~~ alkyl group having 1 to 6 carbons, a substituted or unsubstituted aryl group having 6 to 11 carbons, or a substituted or unsubstituted heteroaryl group (excluding unsubstituted pyridyl groups) having 4 to 10 carbons that may contain one or a plurality of oxygen, nitrogen and sulfur atoms on the ring, in which the substituent represents a halogen atom, OH, NO_2, CN, a linear or branched alkyl group having 1 to 6 carbons, a linear or branched alkoxy group having 1 to 6 carbons (the substituents may be joined to each other at adjacent sites via an acetal bond), a linear or branched alkylthio group having 1 to 6 carbons, a linear or branched alkylsulfonyl group having 1 to 6 carbons, a linear or branched acyl group having 1 to 6 carbons, a linear or branched acylamino group having 1 to 6 carbons, a substituted or unsubstituted anilide group, a trihalomethyl group, a trihalomethoxy group, a phenyl group, an oxo group, a $COOR^3$ group, or a phenoxy group that may be substituted with one or more halogen atoms, and in which the substituents may be independently substituted at any one or more sites of the ring or the alkylene group, ~~with the proviso that J does not represent 2,5-dimethylimidazole-4-yl, when m is 0, A is a single bond, and G represents $-CH_2-$; and further with the proviso that J does not represent unsubstituted, linear or branched alkyl group having 1~~

~~to 6 carbon atoms, when A represents a pyrimidine ring and the position 2 of the pyrimidine ring binds to the methylene adjacent to the S in the formula (1);~~ and

X represents CH or a nitrogen atom;

or a medically acceptable salt thereof.

17. (Amended) A method for preventing ~~and/~~or treating a disease selected from the group consisting of an inflammatory disease, an allergic disease, ~~a disease of the respiratory organs~~bronchial asthma, a disease of circulatory organs selected from the group consisting of sclereosing vascular lesions, intravascular stenosis, disturbances of peripheral circulation, renal failure and cardiac failure, and a disease of bone/cartilage metabolism selected from the group consisting of rheumatoid arthritis and osteroarthritis comprising administering to a human subject ~~a biologicallyan~~ effective amount of a composition comprising a thiobenzimidazole compound as an active ingredient represented by the following formula (1):



(1)

wherein,

R^1 and R^2, simultaneously or independently of each other, represent a hydrogen atom, a halogen atom, a trihalomethyl group, a cyano group, a hydroxy group, an alkyl group having 1 to 4 carbons or an alkoxy group having 1 to 4 carbons, or R^1 and R^2 together form -O-CH_2-O-,

-O-CH_2-CH_2-O- or -CH_2-CH_2-CH_2-, in which the carbons may be substituted with one or a plurality of alkyl groups having 1 to 4 carbons;

A represents a single bond, a substituted or unsubstituted, linear or branched alkylene group having 1 to 6 carbons, a substituted or unsubstituted arylene group having 6 to 11 carbons, or a substituted or unsubstituted heteroarylene group having 4 to 10 carbons that may contain one or a plurality of oxygen, nitrogen and sulfur atoms on the ring, in which the substituent represents a halogen atom, OH, NO_2, CN, a linear or branched alkyl group having 1 to 6 carbons, a linear or branched alkoxy group having 1 to 6 carbons (the substituents may be joined to each other at adjacent sites via an acetal bond), a linear or branched alkylthio group having 1 to 6 carbons, a linear or branched alkylsulfonyl group having 1 to 6 carbons, a linear or branched acyl group having 1 to 6 carbons, a linear or branched acylamino group having 1 to 6 carbons, a trihalomethyl group, a trihalomethoxy group, a phenyl group, an oxo group, or a phenoxy group that may be substituted with one or more halogen atoms, and in which the substituents may be independently substituted at any one or more sites of the ring or the alkylene group;

E represents $COOR^3$, SO_3R^3, $CONHR^3$, SO_2NHR^3, a tetrazole group, a 5-oxo-1,2,4-oxadiazole group or a 5-oxo-1,2,4-thiadiazole group in which R^3 represents a hydrogen atom, or a linear or branched alkyl group having 1 to 6 carbons;

G represents a substituted or unsubstituted, linear or branched alkylene group having 1 to 6 carbons that may be interrupted with one or a plurality of O, S, SO_2, and NR^3, in which R^3 is as defined above and the substituent represents a halogen atom, OH, NO_2, CN, a linear or branched alkyl group having 1 to 6 carbons, a linear or 15 branched alkoxy group having 1 to 6 carbons

(the substituents may be joined to each other at adjacent sites via an acetal bond), a trihalomethyl group, a trihalomethoxy group, a phenyl group, or an oxo group;

m represents an integer of 0 to 2;

when m is 0 and A is a substituted or unsubstituted, linear or branched alkylene group having 1 to 6 carbons, then J represents a substituted or unsubstituted, linear, cyclic or branched alkyl group having 3 to 6 carbons, a substituted or unsubstituted aryl group having 7 to 9 carbons, a substituted aryl group having 10 to 11 carbons, a substituted or unsubstituted heteroaryl group (excluding unsubstituted pyridyl groups) having 4 to 10 carbons that may contain one or a plurality of oxygen, nitrogen and sulfur atoms on the ring~~, with the proviso that J does not represent 2,5-dimethylimidazole-4-yl, when G represents $-CH_2-$~~;

when m is 0 and A is a substituted or unsubstituted arylene group having 6 to 11 carbons or a substituted or unsubstituted heteroarylene group having 4 to 10 carbons that may contain one or a plurality of oxygen, nitrogen and sulfur atoms on the ring, then J represents a substituted or unsubstituted, ~~linear~~, cyclic ~~or branched~~ alkyl group having 1 to 6 carbons, a substituted or unsubstituted aryl group having 6 to 11 carbons, or a substituted or unsubstituted heteroaryl group (excluding unsubstituted pyridyl groups) having 4 to 10 carbons that may contain one or a plurality of oxygen, nitrogen and sulfur atoms on the ring~~, with the proviso that J does not represent unsubstituted, linear or branched alkyl groups having 1 to 6 carbon atoms, when A represents a pyrimidine ring and the position 2 of the pyrimidine ring binds to the methylene adjacent to the S in the formula (1)~~; or

when m is 0 and A is a single bond or when m is 1 or 2, then J represents a substituted or

unsubstituted, ~~linear, cyclic or branched~~ alkyl group having 1 to 6 carbons, a substituted or unsubstituted aryl group having 6 to 11 carbons, or a substituted or unsubstituted heteroaryl group (excluding unsubstituted pyridyl groups) having 4 to 10 carbons that may contain one or a plurality of oxygen, nitrogen and sulfur atoms on the ring, in which the substituent represents a halogen atom, OH, NO_2, CN, a linear or branched alkyl group having 1 to 6 carbons, a linear or branched alkoxy group having 1 to 6 carbons (the substituents may be joined to each other at adjacent sites via an acetal bond), a linear or branched alkylthio group having 1 to 6 carbons, a linear or branched alkylsulfonyl group having 1 to 6 carbons, a linear or branched acyl group having 1 to 6 carbons, a linear or branched acylamino group having 1 to 6 carbons, a substituted or unsubstituted anilide group, a trihalomethyl group, a trihalomethoxy group, a phenyl group, an oxo group, a $COOR^3$ group, or

phenoxy group that may be substituted with one or more halogen atoms, and in which the substituents may be independently substituted at any one or more sites of the ring or the alkylene group~~, with the proviso that J does not represent 2,5-dimethylimidazole-4-yl, when m is 0, A is a single bond, and G represents CH_2; and further with the proviso that J does not represent unsubstituted, linear or branched alkyl group having 1 to 6 carbon atoms, when A represents a pyrimidine ring and the position 2 of the pyrimidine ring binds to the methylene adjacent to the S in the formula (1)~~; and

X represents CH or a nitrogen atom;

or a medically acceptable salt thereof.